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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,650	02/19/2002	Katsumi Fujimoto	14875-101001/C1-107PCT-US	7203

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EXAMINER
MCKELVEY, TERRY ALAN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,650	FUJIMOTO ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7-8 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All objections and rejections not repeated in the instant Action have been withdrawn due to applicant's response to the previous Action.

Election/Restrictions

Claims 7-8 and 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/5/04.

This application contains claims 7-8 and 11-14 drawn to an invention nonelected with traverse in the paper filed 10/5/04. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

Claims 2-4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the

subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 2-4 depend from part of claim 1 (only from part (c) of claim 1) and thus improperly depend from only part of the claim and thus fail to further limit the subject matter of the previous claim. Amending the claims to depend from claim 1 or by making the claims independent claims would be remedial.

Claim Rejections - 35 USC § 101 and 35 USC § 112, First Paragraph

Claims 1-6, 9-10, and 15-19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. This rejection is maintained for reasons of record set forth in the paper mailed 1/3/05 (repeated below and extended to new claims as necessitated by the applicant's amendment filed 7/5/05). Applicants' arguments filed 7/5/05 have been fully considered but they are not deemed to be persuasive.

The claims are directed to isolated nucleic acid selected from the group consisting of nucleic acids: comprising the

coding region of a nucleotide sequence selected from SEQ ID NO:1 and 11 (elected), encoding a protein comprising SEQ ID NO:2 or 12 (elected), encoding a protein comprising a modified amino acid sequence which retains the biological activity of SEQ ID NO:2 or 12, hybridizes under stringent conditions to a sequence selected from SEQ ID NO:1 and 11 and encoding a protein that retains the biological activity of SEQ ID NO:2 or 12, and encoding a partial peptide of a protein selected from SEQ ID NO:2 and 12. Vectors and transformants comprising the nucleic acids are also claimed, as are nucleic acids that comprise 15 or more nucleotides of SEQ ID NO:1 or 11.

There is no well established utility for the nucleic acids and encoded proteins because the nucleic acids and proteins are not completely described in the prior art and there is no specific function taught which is similar enough to a prior art nucleic acid or protein so as to support a well established utility.

The specification discloses that the protein encoded by the nucleic acids fits into a family of bHLH transcription factors each member of which are involved in different aspects of development and differentiation. This identification of the family is based upon only a limited degree of homology. However, the instant specification does not disclose any

additional information regarding the protein such as what cell types express the protein or what the subcellular location is, timing of regulation of the protein during cellular differentiation, which hormones or transcription factors regulate the protein, and what physiological or biochemical significance is possessed by the protein, such as what the target sites of the alleged transcription factor are. The specific biological activity of the protein and variants and fragments of the protein encoded by the nucleic acids as claimed are not taught.

The specification asserts the following utilities for the claimed nucleic acids, etc:

1. used as marker to determine developmental stages and cell differentiation.

2. used for diagnosis of diseases associated with the protein encoded by the nucleic acids.

3. used for prophylaxis and treatment of diseases associated with the protein encoded by the nucleic acids (i.e., gene therapy using the nucleic acids).

4. used in the development of pharmaceutical agents for various diseases associated with the protein.

5. used for in vivo or in vitro production of the protein, which protein can be used for purposes similar to those above,

and for screening for a compound that binds to the protein which is a potential therapeutic for the diseases associated with the protein.

However, none of these asserted uses meet the three-pronged requirement of 35 USC 101 regarding utility, namely, that the asserted utility be credible, specific, and substantial. The asserted utilities will each be addressed in turn.

1. The specification does not teach what the specific developmental stages or cell differentiation is associated with the nucleic acid or protein and thus this asserted utility is not specific or substantial. Any protein or nucleic acid can potentially be a marker, but in the absence of the specific association of the nucleic acid or protein with a particular stage or differentiation state, there is no specificity and significant further experimentation is required to confirm the real world context of use of the nucleic acids as a marker for a stage or cell state.

2. and 3. The specification does not teach any specific disease that is specifically affected by the claimed nucleic acid or encoded protein. Although it is indicated that the protein may be associated with cartilages and arthritis, this is not a substantial utility because no specific nexus between this assertion and the claimed nucleic acids and encoded protein is

taught. It would require significant further experimentation to confirm that the nucleic acid and protein is associated with what is alleged based upon no evidence showing the actual association with the indicated diseases or tissues. Thus, use of the nucleic acids or encoded proteins for diagnosis or prophylaxis or treatment would require significant further experimentation to confirm the real world context of use for any of these uses.

4. Because the specification does not demonstrate that the nucleic acids and encoded proteins are specifically associated with any particular disease, there is no specific utility for developing pharmaceuticals based upon the nucleic acids or encoded proteins because any nucleic acids or proteins can be potentially used for development of pharmaceuticals, without specificity to a specific disease that is associated with the nucleic acids or encoded proteins. The utility is not substantial because significant further experimentation would be required to confirm the real world use of the nucleic acids or encoded proteins in making pharmaceutical agents.

5. The specification teaches that the nucleic acids can be used for the production of the encoded proteins. First, this is not true for all of the nucleic acids claimed. Second, this a specific, substantial, and credible utility only if the produced

protein has a specific, substantial, and credible utility. Most of these asserted utilities are addressed above. The specification also asserts that the protein can be used for screening for a compound that binds to the protein which is a potential therapeutic for the diseases associated with the protein. This is not a specific and substantial utility for essentially the same reasons set forth in item 4 above.

Claims 1-6, 9-10, and 15-19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. This rejection is maintained for reasons of record set forth in the paper mailed 1/3/05 (and extended to new claims as necessitated by the applicant's amendment filed 7/5/05). Applicants' arguments filed 7/5/05 have been fully considered but they are not deemed to be persuasive.

Response to Arguments

The applicants argue that they have made an assertion of (multiple) utilities for the invention. This argument is not

persuasive in overcoming the instant rejection because each of these asserted utilities were addressed in the rejection and none of them were found to be specific, substantial, and credible.

The applicants argue that claim 1 is similar to Example 10 of the Utility Guidelines (which example is drawn to having a high homology to DNA ligase). This argument is not persuasive because it is not questioned that the claimed nucleic acid encodes a protein that is likely a bHLH transcription factor. However, unlike ligases in which the enzymatic activity is defined and can be clearly used by any protein having that activity because a ligase has a specific, substantial, and credible utility, even though bHLH transcription factors have related structures, they have very different specific activities because each family member regulates the expression of different genes which then affect different cellular processes (e.g., myogenesis, neurogenesis, and hematopoiesis). Each family member does not have all of these activities, but instead has specific activities that are very different from the other family members. So, unlike ligase, once a member of the bHLH transcription factor is identified, one would not know what specific activity it has in the absence of empirically determined data.

The applicants argue that the utility is further substantiated by Azmi et al which demonstrates that marine Sharp-1 inhibits skeletal muscle differentiation. This argument is not persuasive because this utility was not specifically asserted for the protein encoded by the claimed nucleic acid in the application as filed. Second, because each family member of the bHLH transcription factor family has a different regulatory activity, determining the activity of one family member does not result in the determination of the activity of another family member such as the instantly claimed protein. Even though there is a region of high similarity between the claimed protein and marine Sharp-1, the claimed protein has at least about 30% additional sequences that are not present in Sharp-1. Thus the claimed protein likely has a much different activity. This is like other bHLH transcription factor family members each of which have a different specific activity, even though they all are in the very broad class of transcription factors.

The applicants argue that the asserted utility is specific because not all transcription factors are expected to control development and tissue differentiation. This argument is not persuasive because controlling development and tissue differentiation is not specific because literally hundreds or thousands of very different genes control development and tissue

differentiation in very different ways. Unlike ligases, their activities are not exchangeable because each gene that controls development and tissue differentiation does so in very different and specific ways. The specific way in which the claimed protein controls development and differentiation is not taught in the art or specification and thus in the absence of such information one skilled in the art would not know in what way the claimed protein controls development and tissue differentiation and thus the asserted utility is not specific.

The applicants argue that the asserted utility is a substantial utility because it defines a real world use: the protein is expected to control development and tissue differentiation, and given their role in differentiation of cartilaginous tissues, they can be used for screening for substances in treating conditions such as osteoarthritis. This argument is not persuasive because controlling development and tissue differentiation is too generic of a utility to be used in the absence of the identification of which specific cells are affected (and how they are affected) during development and what tissues (and how the tissues are) affected during differentiation. In order to determine and confirm the specific real world use of the claimed protein, one would have to conduct significant further experimentation to identify and confirm

which cells and tissues are affected (and how they are affected) during development and tissue differentiation. Therefore, the asserted utility is not substantial. Although it is indicated by the applicants that the protein may be associated with cartilages and arthritis, this is not a substantial utility because no specific nexus between this assertion and the claimed nucleic acids and encoded protein is taught and it would require significant further experimentation to identify how the protein is involved in cartilages and arthritis and then confirm its specific real world use.

The applicants argue that the asserted utility is credible. This argument is not persuasive in overcoming the instant rejection because no argument was made that the asserted utility was not credible.

The applicants argue that the utility of the nucleic acid fragments have utility as a probe or primer to identify the full length sequence. This argument is not persuasive in overcoming the instant rejection because the probe or primer utility relies upon the utility of the full length sequence for its specific, substantial, and credible utility. Because the full length sequence lacks specific and substantial utility for the reasons described above, the fragments of the nucleic acid also lack

specific and substantial utility for the reasons described above.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify

applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

October 3, 2005